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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,976	06/20/2000	WILFRIED L J DALEMANS	B45124	6694
20462	7590	01/27/2004	EXAMINER	
SMITHKLINE BEECHAM CORPORATION CORPORATE INTELLECTUAL PROPERTY-US, UW2220 P. O. BOX 1539 KING OF PRUSSIA, PA 19406-0939			LI, BAO Q	
			ART UNIT	PAPER NUMBER
			1648	
DATE MAILED: 01/27/2004				

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Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/581,976	DALEMANS ET AL.
	Examiner Bao Qun Li	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 12/17/2003.

2a) This action is FINAL.      2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1,3-11 and 13-15 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1,3-11 and 13-15 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 12/17/2003 is/are: a) accepted or b) objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. §§ 119 and 120

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

    1. Certified copies of the priority documents have been received.

    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.

    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

13) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) The translation of the foreign language provisional application has been received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) 32.

4) Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_.

5) Notice of Informal Patent Application (PTO-152)

6) Other: \_\_\_\_\_

### **DETAILED ACTION**

Claims 1, 3-11 and 13-15 are pending and considered before the examiner.

#### **RCE**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application on October 32, 2003. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the previous Office Action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 31, 2003 has been entered. The RCE follows:

#### ***Drawings***

2. The drawings were received on October 31, 2003. The Office accepts these drawings.

#### ***Information Disclosure Statement***

3. The supplemental information disclosure statement (IDS) submitted on October 31, 2003 was filed after the mailing date of the Notice Allowance on July 28, 2003. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

#### ***Response to the amendment***

4. The amendment of sequence listing and claims 1 and 15 for correcting the typo mistakes that are filed on 12/17/2203 have been viewed by examiner and entered.

5. Upon carefully reconsidering the pending claims, there are some claims still subjected to have *35 USC § 112* issues need to be resolved before the application is in condition for allowance on the record. Examiner apologizes these issues were overlooked by the examiner, which may bring some inconvenience for the Applicants.

#### ***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

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7. Claims 1, 3-11 and 13-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 1 and 15 are vague and indefinite in that the metes and bounds of "T helper epitope" are not defined. Although the claims are interpreted in light of the specification, and the specification does not give the definition of what the recited "T helper epitope" is. This rejection affects the dependent claims 3-11 and 13-14.

***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1, 3-11 and 13-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

11. In the instant case, the specification only teaches that the first 1/3 of N-terminal amino acids of influenza virus lipoprotein D and N-terminus of 1-81 amino acid residues of influenza virus NS1 protein are used as the fusion partner (See lines 26-29 on page 5). However, the specification does not describe any other fragment having a T epitopes.

12. Regarding to this written description rejection, Applicants are remaindered to See

13. *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed, Cir. 1997):

The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention .... and at pg 1406: a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others,

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except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

14. See also *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021: A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

15. The case law of *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016, which teach that the disclosure of a process for obtaining cDNA and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

16. 35 USC 112 requires *inter alia* that "a patent specification contain a written description of the invention and the manner and process of making and using it in such full, clear, and concise terms as to enable one skilled in the art to make and use the invention".

17. While applicants previously amended the claims by adding the functional limitation of "T helper epitope", and asserted that this fictional limitation will render the 112 2<sup>nd</sup> paragraph rejection moot. However, after reconsidering the claimed products and method of using the same, the amendment still does not help for the claims in that the precise structure of claimed products in question are still undesirable and unknown. Therefore, the claims are rejected.

#### ***Claim Rejections - 35 USC § 112***

18. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly

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connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a variety of composition comprising E6 or E7 protein or E6/E7 fusion protein of HPV16 or HPV18 operably linked to a fusion partner of the lipoprotein D (Ser 20-Thr 127) of *Haemophilus influenza B* that is further fused with a histidine tag, wherein the composition also comprises an immunomodulatory oligodexynulceotide CpG motif as an adjuvant to produce an immune response against tumor antigen of E6 and E7, does not reasonably provide enablement for having a method of using the composition for preventing the tumor development. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

20. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See *United States v. Theketronic Inc.*, 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and *gair in re Wands*, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

21. 1) & 2) State of Art and Unpredictability.

22. The state of art teaches that human papillomavirus (HPV) E6 and E7 is a tumor rejection antigen as evidenced by Chen et al. (Pro. Natl. Acad. Sci. USA, 1991, Vol. 88, pp. 110-114. However, It is known in the art that the E7 or E6 is not a strong antigen, and it usually produces a weak immune response by itself without the combination with other HPV antigen(s). CpG motif is a short nucleotide sequence that has an adjuvant activity. However, not every CpG motif can have such immunostimulating activity as evidenced by Yamamoto et al. (*Immunobiology of Bacterial CpG-DNA*, pp. 26-27, see the section 3.1 and 3.2). He teaches that although the hexamer palindromic sequences having -CG- motif are essential for inference (IFN) production and Nature Killer cell (NK) augmentation, some exceptional cases still exist. For instance, GTCGTT and GACGTT are active, whereas GACGTC is inactive (pp. 30, 2<sup>nd</sup> paragraph). It is

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also true that formula, purine purine cytosin quanine pyrimidine pyromidine (Pu-Pu-CG-Py-Py), which has been used wildly by many investigations, has many exceptions (pp. 31, 2<sup>nd</sup> paragraph). Even in the present case, the specification only shows that 1 out of 3 such oligonucleotide increases the CTL activity against the E7/HPV16 antigen and causes a partial tumor regression. Nevertheless, no E1 and/or E7 immunogenic composition has been approved as a tumor vaccine. Therefore, the method of using the claimed composition for preventing HPV induced cancer is unpredictable.

23. 3) & 4) Number of working examples and Amount of guidance.

24. In the instant case, the specification only discloses that the immunogenic compositions are made by E6 or E7 or E6/E7 HPV16 of HPV18 or HPV 16 fused with amino acid residues ser 20-Thr 127 of mature protein D of haemophilus influenza virus [Prot-D1/3-E7-His/HPV16 (TCA308), Prot-D1/3-E6-His/HPV16 (TCA307), Prot-D1/3-E6/E7-His/HPV16 (TCA311), Prot-D1/3-E7-His/HPV18 TCA313), Prot-D1/3-E6-His/HPV18 (TCA314), Prot-D1/3-E7-His/HPV18 (TCA328)], and administration of the composition of TCA308 in combination with an immunomodulatory oligonucleotide CpG 1826 produces an enhanced activity of Cytotoxic T Lymphocyte (CTL) against E7 antigen of HPV16, which results in a partial tumor regression and a weak antibody response.

25. However, the specification is deficient for teaching that the claimed composition can be used as a vaccine for preventing HPV induced tumor development.

26. 5) & 6) Scope of claims and Nature of the invention.

27. The scope of claimed invention broadly read on a method for using the claimed composition for preventing the HPV induce tumor. The nature of the invention related to the tumor vaccine.

28. 7) Lever of the skill in the art.

29. The level of the skill in the tumor vaccine development is very high. It requires a challenge assay in a suitable animal model to approve that the claimed composition can be used for preventing PHV induced tumor.

30. Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan

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would have had to conduct undue and excessive experimentation in order to practice the claimed invention.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li

January 13, 2004

  
JAMES C. HOUSEL  
JAMES HOUSEL  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600  
1/26/04